

# Effects of Health-Promoting Lifestyle on Late-Onset Depression in Older Adults: Mediating Effect of Meaning in Life and Interleukin-6 (IL-6)

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**Purpose:** Late-onset depression (LOD) with poor treatment response has high incidence and mortality in the China's aged people, this study aims to explore the correlation between health-promoting lifestyle, meaning in life, interleukin-6 (IL-6) and LOD for providing scientific basis of LOD prevention and rehabilitation.

**Patients and Methods:** A total of 496 LOD patients (study group) and healthy older adults (control group) were enrolled and investigated by using the Health-promoting lifestyle Profile-II, revised (HPLP-IIR), Meaning in Life Questionnaire-Chinese Version (MLQ-C), and Hamilton Depression Scale (HAMD). The interleukin-6 (IL-6) in the circulating blood was detected by utilizing ELISA kit.

**Results:** The results showed that the scores of all factors in HPLP-IIR and MLQ were significantly lower and IL-6 level was higher in the study group than the control group. Scores of most factors in HPLP-IIR and MLQ negatively and IL-6 positively correlated with scores of subscales and total HAMD score. Meaning in life and IL-6 partially mediated the relationship between health-promoting lifestyles and depression severity in the study group, with the mediating effect explains 15.76% and 22.64% of the total effect, respectively.

**Conclusion:** Health-promoting lifestyles, meaning in life, and IL-6 are predictors of LOD, and an unhealthy lifestyle could induce LOD through the mediating effect of meaning in life and IL-6 in older adults.

**Keywords:** late-onset depression, meaning in life, health-promoting lifestyle, older adult

## Introduction

Late-onset depression (LOD) specifically indicates first-onset major depression that is not due to another medical condition of physical disease or (or) medical abuse in older adults (aged 60 years or older). Previous studies have found that LOD is usually associated with high disability and mortality, and the treatment response of conventional antidepressants is poor in more than 50% of patients with LOD; at the same time, LOD is strongly correlated with common diseases such as mild cognitive impairment (MCI), Alzheimer's disease (AD), and stroke in older adult.<sup>1-3</sup> Therefore, the exploration of the treatment, prevention, rehabilitation, and pathological mechanisms of LOD are of great concern worldwide. According to the existing literature, LOD has both the common features of depressive disorders and specificity in terms of symptoms, etiology, and pathological mechanisms. The common feature is that LOD is consistent with subtypes of depressive disorders (major depressive disorder, disruptive mood dysregulation disorder, dysthymia, etc.) in the symptoms of sad, empty, irritable mood, somatic complaints, cognitive impairments and etiology of stressors, genetic susceptibility, and maladaptive personality traits. Besides, specificity refers to the fact that LOD is often associated with brain aging, cerebrovascular disease, and sleep disorders (eg, sleep apnea syndrome).<sup>4,5</sup>

Health-promoting lifestyle is defined as spontaneous, multifaceted behavioral habits and mental experiences of self-actualization and self-identity to improve health and quality of life. Previous studies have shown that health-promoting lifestyles, including health responsibility, social support, regular exercise, reading habits, stress management, nutrition balance, strongly related to control of blood sugar and blood pressure, improvement of sleep quality and may further reduce the LOD occurrence in older adult.<sup>6-8</sup> Meaning in life is considered as one type of personality trait that bases the foundation for subjective well-being and also broadly described as the individual's identification, pursuit for existence value and motivation to pursue the insight of human life and to establish life purpose.<sup>9</sup> George and Park in one systematic review argued that there were two barriers impede research of meaning in life: No consensus definition for the construct and no integration of research area, a tripartite view of meaning in life, as composed of three distinct subconstructs—comprehension, purpose, and mattering—has recently been gaining momentum, it is believed that this tripartite view could add clarity to the literature as it outlines three more specific and targeted subconstructs without lumping them together into a singular more diffuse concept.<sup>10</sup> Meaning in life is acknowledged to be a central human concern in temporary psychology for its key role in not only psychosocial functioning but also in survival, it is thought that poor psychosocial function or mental symptoms, such as hopelessness, distress, anxiety, insomnia, and suicidal ideation, tend to arise when there is a lack of meaning in life.

Many elderly people may become “empty nesters” in the accelerating process of China's urbanization, a survey conducted by Wei found that the phenomenon of “empty nest” in community retirees is common with total rate and absolute rate of 61.63%, 27.91%, respectively. Psychosomatic disorder in absolute empty nesters is more severe than in groups of relative empty-nest and the non empty-nest. Some older adults, described as a group of migrants in cities with their sons or daughters, often take on the task of caring for grandchildren. It is necessary for them to gradually adapt to and integrate into urban life. Typical features of urban life, including large population mobility, small living scope, low involvement in interpersonal communication, high job stress. A previous study has proved that relationship quality and attachment style are significantly related to individuals' mental and physical health. Another study conducted by Chen explored the factors associated with quality of life in the elderly from the perspective of social ecology and showed that unstable interpersonal relationships can directly affect life quality and meaning in life has a moderating effect between unstable interpersonal relationships and life quality.<sup>11,12</sup> It is believed that unhealthy-promoting lifestyle may be increased on the condition of loneliness, social alienation and maladjustment.

At the same time, most elderly people, who enters their retirement stage with great changes in social role, social status, power, life content, are more likely to experience worthlessness, self-denial, emptiness, thwarted belongingness and become susceptible to LOD for the lack of meaning in life. It is shown in clinical practice that missing of meaning in life in almost all domains may be the core symptom of LOD and routine drug treatment and physiotherapy have no significant improvement on LOD patients' loss of meaning in life. Some researchers have discussed the effects of psychological interventions on the meaning of life, for example, a study conducted by Li reported that mindfulness meditation combined with painting decompression could improve mood state, sense of coherence, and life-significance construct in patients with acute ischemic stroke. Another study found that Satir's model group intervention could effectively enhance college students' sense of meaning in life.<sup>13,14</sup> Based on these results, it can be concluded that psychological interventions may be an effective way to enhance their sense of meaning in life. However, compared with other treatment strategies, psychological intervention is characterized with large investment, slow therapeutic response, and high insight requirements of patients, which often limit its clinical application. Therefore, it is still urgent to explore associated factors of meaning in life for improving LOD prevention programs.

Some recent studies found that health-promoting lifestyle positively associated with self-acceptance, family cohesion and adaptability, social support and negatively correlated with self-neglect.<sup>15,16</sup> It is considered that good quality of self-acceptance, family cohesion and adaptability, and social support may be the main mental constructs of meaning in life,<sup>17,18</sup> that is, the cultivation of health promoting lifestyles may be a potential strategy for enhancing meaning in life that could further prevent or attenuate LOD, hence, it can be hypothesized that meaning in life exerts a mediating role between health-promoting lifestyle and LOD.

The onset, treatment, rehabilitation, relapse of depressive disorder (DD) is also a complicated pathobiology process with alteration in neurophysiology and immunocyto chemistry, more and more studies shed light on the role of cytokine,

especially the interleukin-6 (IL-6), in stress-related psychopathology of DD, it has been verified that the elevation of IL-6 level is not only observable in acute DD patients but also in patients after remission, higher-circulating level of IL-6 may relate to attenuated daytime heart rate variability (HRV) that often considered as biological cardiac risk factor for DD and severe childhood trauma that strongly associated with DD.<sup>19,20</sup> Some previous studies suggest that lifestyles, including smoking, physical activity, dietary habits, sleep disturbance, unsuccessful stress management were associated with specific cytokines of IL-6 in healthy subjects,<sup>21,22</sup> it may be a great concern whether health-promoting lifestyle could lower the IL-6 level and further ameliorate the LOD. So, the second hypothesis can be proposed that IL-6 is the mediator between health-promoting lifestyle and LOD.

In summary, this study aimed to explore the relationship between LOD and health-promoting lifestyle, meaning in life, and IL-6 for providing a scientific basis for community prevention and rehabilitation of LOD.

## Materials and Methods

### Participants

#### Study Group

A total of 496 LOD patients, 226 males and 270 females, aged 60–73 years, were enrolled from outpatient or inpatient at our hospital from January 2017 to December 2022 by convenience sampling. The following are the inclusion criteria for LOD patients: LOD patients must meet the diagnostic criteria and differential diagnosis for major depressive disorder in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V), all of whom were first cases of LOD with no other serious mental disorders or disease history and had basic skills in reading, understanding, and writing. Patients with serious physical diseases (diabetes, cardiovascular and cerebrovascular diseases, brain trauma, etc.), psychosocial function disability, experience of severe mental-trauma event in the past six months (eg, death of spouse, divorce, serious accidents, etc.), a history of psychoactive substance abuse, and treatment history of antidepressant, physical therapy, psychotherapy in the past were excluded.

#### Control Group

A group of 496 healthy elderly people (254 males and 242 females, aged 62–71 years) were continuously recruited from community residents by convenience sampling. The Inclusion criteria were as follows: No history of serious mental disorders (schizophrenia, anxiety disorder, obsessive-compulsive disorder, etc.); No reports of psychosocial function disability; no stroke, traumatic brain injury, endocrine system disease, or personal disease history that may affect nervous system function; and no mental trauma exposure in the past 6 months. The participants reported history of depressive disorder who received antidepressant, physical therapy, psychotherapy were excluded.

The approved cut-points of Hamilton Depression Scale (HAMD) in Chinese population are as follows: HAMD score > 35, severe; >20, moderate; <8, no depressive disorder. In the present study, HAMD score in LOD patients >20 and in healthy controls <8.<sup>23</sup>

### Assessment Scales

#### Health-Promoting Lifestyle Profile-II, Revise (HPLP-IIR)

Forty items of HPLP-IIR, scored with “1 (never) to 4 (always)” points, were assigned into six factors of interpersonal relation (IR), health responsibility (HR), stress management (SM), nutrition (N), physical activity (PA) and spiritual growth (SG). The higher the score, the better the health promoting lifestyle.<sup>24</sup> The Cronbach’s  $\alpha$  of the HPLP-IIR in this study was 0.852.

#### Meaning in Life Questionnaire-Chinese Version (MLQ-C)

Meaning in Life Questionnaire was initially developed by Steger and widely utilized around the world. The MLQ-C had 10 items, which were scored on a scale of “1 (completely inconsistent) to 7 (completely consistent)” and were divided into two factors: Presence of Meaning (PM) and Search for Meaning (SM). A higher score indicated a stronger sense of meaning in life.<sup>25,26</sup> The Cronbach’s  $\alpha$  of the MLQ-C in this study was 0.789.

## Hamilton Depression Scale (HAMD)

The Chinese version of the HAMD consisted of 24 items, was divided into seven dimensions: Anxiety/somatization (AS), weight (W), cognitive disorder (CD), diurnal variation (DV), retardation (R), sleep disturbance (SD), and hopelessness (H). It was widely used in the clinical practice and scientific research of psychiatry to assess the depression severity with good property of reliability, validity, a higher score suggested that LOD was more severe.<sup>23</sup> The Cronbach's  $\alpha$  of HAMD in this study was 0.893.

Based on the diagnosis of the attending physician and the inclusion criteria, all participants were assessed using the HPLP-IIR, MLQ-C, and HAMD. General demographic data (eg, sex, marital status, educational level, and disease history) were recorded during the psychological test.

## IL-6 Test

Whole blood (5 mL) was collected into EDTA-containing anticoagulant tubes between 7:00 a.m. and 9:00 a.m. Next, the serum was isolated from whole blood at a low temperature of 4 °C and 3000 rpm for approximately 10 min, and then add the prepared species and standard product into the isolated serum to react for 30 min at 37 °C. TMB chromogen solutions A and B were added for color display at 37 °C for 10 min after washing the plate five times. Finally, a termination solution was added, and the optical density (OD) value was measured within 5 min. Lastly, the IL-6 were detected by using an enzyme-linked immunosorbent assay (ELISA kit, purchased in Shanghai Mingfeng Biological Co., Ltd., Shanghai, China, Art. No. M-10711, M-10080). All experimental procedures were performed following the Application Instruction (AI) provided with the manufacturer's instructions.

## Statistical Processing

SPSS21.0 is employed for data analysis. Chi-square test ( $\chi^2$ ), Independent sample *t*-test were used to compare between-group differences in demographic characteristics, health promoting lifestyle, meaning in life, and IL-6 level. Pearson's correlation and multiple-regression analyses were used to verify the relationship between health promoting lifestyle, meaning in life, IL-6, and LOD in the elderly. Statistical significance was set at  $P < 0.05$ .

## Results

### Descriptive Statistics

Table 1 shows the demographic characteristics of study and control group. There were no significant differences of gender and age between LOD patients and healthy controls ( $P > 0.05$ ).

### Between-Group Comparison of Health-Promoting Lifestyle, Meaning in Life, IL-6

As can be seen in Table 2, the scores of all factors in HPLP-IIR and MLQ-C in LOD patients were lower and IL-6 level was higher significantly than those in the healthy controls ( $P < 0.01$ , or 0.001) (see Table 2).

**Table 1** Between-Group Comparison of Demographic Characteristics (%/ $\bar{x} \pm SD$ )

Variables	Study Group (N =496)	Control Group (N =496)	$\chi^2/t$	P
Gender				
Female	226	270	3.16	0.080
Male	254	242		
Age	66.05 $\pm$ 3.35	66.41 $\pm$ 3.30	-1.68	0.093

Note:  $\chi^2$  is Chi-square test.

**Table 2** Comparison of Health-Promoting Lifestyle, Meaning in Life, IL-6 Between Study Group and Control Group ( $\bar{x} \pm SD$ )

Factors	Study Group (n=496)	Control Group (n=496)	t	Cohen's d	P
IR	11.28±4.09	12.27±2.96	-4.39	0.277	<0.001
HR	22.52±8.27	25.38±5.97	-6.27	0.397	<0.001
SM	11.35±4.24	12.80±3.15	-6.10	0.388	<0.001
N	12.73±4.77	13.54±3.83	-2.95	0.187	<0.01
PA	17.63±6.35	19.65±5.14	-5.53	0.350	<0.001
SG	10.99±4.31	13.10±3.16	-8.83	0.558	<0.001
PM	24.98±8.17	27.98±4.18	-7.32	0.462	<0.001
SM	27.05±6.43	29.99±2.97	-9.28	0.756	<0.001
IL-6	35.22±32.13	30.21±29.32	2.57	0.155	<0.01

**Abbreviations:** IR, interpersonal relation; HR, health responsibility; SM, stress management; N, nutrition; PA, physical activity; SG, spiritual growth; PM, Presence of Meaning; SM, Search for Meaning; IL-6, interleukin-6.

### Pearson Correlation for Health-Promoting Lifestyle, Meaning in Life, IL-6 Level, and Depression Severity in Study Group

Correlation analysis suggested that most factors of HPLP-IIR and MLQ negatively and IL-6 positively correlated with scores of subscales and total HAMD score ( $P < 0.05$  or  $0.01$ ) (see Table 3).

### Mediating-Effect Analysis of Meaning in Life and IL-6 Between Health-Promoting Lifestyle and Depression Severity in the Study Group

According to test procedure for mediating effect proposed by Wen,<sup>27</sup> hierarchical regression analysis was used to test the mediating effect of meaning in life and IL-6 between health-promoting lifestyles and depression severity. The following three steps of regression analysis were conducted: Step 1, the total score of HPLP-IIR was used as the predictor variable, and of HAMD as the dependent variable; Step 2, the total score of HPLP-IIR was the predictive variable, and of MLQ and IL-6 were the dependent variables, respectively; Step 3, The total scores of HPLP-IIR and MLQ or IL-6 were performed as predictive variables respectively, and of HAMD as dependent variable. From the direct effect to the mediating model, the total score of HPLP-IIR still significantly predicted the total score of HAMD ( $P < 0.001$ ), but the path coefficient became smaller which indicated that meaning in life and IL-6 played a partial mediating role between health promoting lifestyles and depression severity in the study group. The mediating effects of meaning in life, IL-6 were  $0.151 \times 0.166 = 0.025$  and  $0.168 \times 0.214 = 0.036$  respectively, while meaning in life explained 15.76% ( $0.151 \times 0.166 / 0.159$ ) and IL-6 explained 22.64% ( $0.168 \times 0.214 / 0.159$ ) of the total effect in the mediating model (see Tables 4 and 5).

**Table 3** Pearson Correlation for Health-Promoting Lifestyle, Meaning in Life and Depression Severity in Study Group (r)

Factors	AS	W	CD	DV	R	SD	H	HAMD
IR	-0.38**	-0.20**	-0.37**	-0.18**	-0.34**	-0.31**	-0.31**	-0.57**
HR	-0.44**	-0.16**	-0.43**	-0.18**	-0.37**	-0.32**	-0.35**	-0.65**
SM	-0.40**	-0.18**	-0.41**	-0.17**	-0.39**	-0.31**	-0.36**	-0.63**
N	-0.38**	-0.16**	-0.38**	-0.17**	-0.38**	-0.35**	-0.31**	-0.60**
PA	-0.41**	-0.11*	-0.43**	-0.20**	-0.38**	-0.29**	-0.37**	-0.65**
SG	-0.42**	-0.17**	-0.43**	-0.22**	-0.41**	-0.31**	-0.36**	-0.67**
PM	-0.22**	-0.22**	-0.37**	-0.08	-0.18**	-0.16**	-0.42**	-0.44**
SM	-0.31**	-0.24**	-0.38**	-0.05	-0.20**	-0.19**	-0.40**	-0.49**
IL-6	0.238**	0.151**	0.221**	0.038	0.247**	0.092*	0.213**	0.356**

**Note:** r is correlation coefficient, \* is  $P < 0.05$ , \*\* is  $P < 0.01$ .

**Abbreviations:** IR, interpersonal relation; HR, health responsibility; SM, stress management; N, nutrition; PA, physical activity; SG, spiritual growth; PM, Presence of Meaning; SM, Search for Meaning; IL-6, interleukin-6; AS, anxiety/somatization; W, weight; CD, cognitive disorder; DV, diurnal variation; R, retardation; SD, sleep disturbance; H, hopelessness; HAMD, Hamilton Depression Scale.

**Table 4** Mediating-Effect Analysis of Meaning in Life Between Health-Promoting Lifestyle and Depression Severity

Step	Dependent Variable	Independent Variable	$\beta$	t	P
Step 1	Total score of HAMD	Total score of HPLP-IIR	-0.159	-19.02	<0.001
Step 2	Total score of MLQ-C	Total score of HPLP-IIR	0.166	8.69	<0.001
Step 3	Total score of HAMD	Total score of HPLP-IIR	-0.134	-15.88	<0.001
		Total score of MLQ-C	-0.151	-8.16	<0.001

**Note:**  $\beta$  is standardized regression coefficient.

**Abbreviations:** HAMD, Hamilton Depression Scale; HPLP-IIR, Health-promoting lifestyle Profile-II revise; MLQ-C, Meaning in Life Questionnaire-Chinese Version.

**Table 5** Mediating-Effect Analysis of IL-6 Between Health-Promoting Lifestyle and Depression Severity

Step	Dependent Variable	Independent Variable	$\beta$	t	P
Step 1	Total score of HAMD	Total score of HPLP-IIR	-0.159	-19.02	<0.001
Step 2	IL-6	Total score of HPLP-IIR	-0.168	8.69	<0.001
Step 3	Total score of HAMD	Total score of HPLP-IIR	-0.147	-17.52	<0.001
		IL-6	0.214	5.99	<0.001

**Note:**  $\beta$  is standardized regression coefficient.

**Abbreviations:** HAMD, Hamilton Depression Scale; HPLP-IIR, Health-promoting lifestyle Profile-II revise; IL-6, interleukin-6.

## Discussion

According to China's 7th National Census released in 2021, the population aged 60 years and above accounts for 18.70% of the total population which clearly indicates that the aging of the Chinese population has further deepened. On the background of population aging, LOD, which has a high prevalence, is a serious threat to quality of life and life expectancy in older adults. Therefore, the exploration of the etiology and pathology of LOD has become an urgent issue for effectively coping with population aging.

Firstly, the present study found that the scores of HPLP-IIR and MLQ-C in LOD patients were lower than the healthy controls, and scores of most factors of HPLP-IIR and MLQ were negatively correlated with scores of AS, CD, R, SD, H, and total score of HAMD, these results showed that health-promoting lifestyles and meaning in life are predictors of LOD in the elderly. Health-promoting lifestyles, usually associated with the social cultural background and personnel behavioral habits, could orientate individuals, families, communities, and the whole society to good quality of self-harmony, subjective well-being, self-actualization, fitness keeping, sense of belonging to a larger social group.<sup>28,29</sup> Previous studies have shown that unhealthy promoting lifestyles are common in modern people, such as lack of exercise, staying up late, addiction to Internet games or short videos, and junk food intake, which not only greatly reduced the opportunities for interpersonal interaction in reality and closeness to nature, but also increased the incidence of behavioral addiction, obesity and impaired structure and function in the limbic system,<sup>30-34</sup> those may result in a high risk of LOD in the elderly. Meaning in life, as a positive personality trait, is the identification and pursuit of life values integrated with social progress goals or self achievement. Meaning in life is often associated with readjustment and mental resilience after exposure to trauma and alleviated anxiety by increasing adaptive coping styles, reducing avoidant behavior, and improving stress coping ability. Sense of life meaning, which is strongly related to goal orientation and behavioral motivation, can also diminish feelings of hopelessness and spiritual emptiness,<sup>35-37</sup> thus it may lower the incidence of LOD in older adults.

The mediating effect analysis of the meaning in life between health-promoting lifestyles and LOD in the study group showed that meaning in life plays a partial-mediating role between health-promoting lifestyles and LOD severity which means the health-promoting lifestyles can indirectly improve depressive symptoms by the pathway of raising meaning in life. Health-promoting lifestyles can strengthen the sense of self-affirmation and self-control for buffering the impairment of low socioeconomic status on self-identity in older adults and that a health-promoting lifestyle can improve social support by reducing social alienation and enhancing group belonging and sense of security. To some extent, a health-

promoting lifestyle is a great protective factor for chronic diseases (eg, diabetes and hypertension) and further improves life quality,<sup>38–40</sup> older adults may have more sense of meaning in life consisted of self-worth, hope diathesis, and high self-efficacy and thereby LOD severity is attenuated.

Secondly, this study showed that IL-6 level in the study group was higher than the healthy controls, and positively correlated with scores of AS, W, CD, DV, R, SD, H and total score of HAMD. This is consistent with some previous published literatures, which show that physiological IL-6 signaling preserves neurogenesis, neuronal differentiation, neuroprotection against tissue injury and the pathological outcomes of IL-6 are related to its pleiotropic effects in the brain by microglia, astrocytes, neurons, endothelial cells, and peripheral infiltrating macrophages or T lymphocytes. These physiological processes could evidently change the brain function and ultimately induce LOD in older adults.<sup>41,42</sup> Mediating effect analysis suggests IL-6 partially mediates the relationship between health-promoting lifestyle and depression severity in study group, which signifies health-promoting lifestyle could improve LOD by decreasing IL-6 level. Some recent studies showed that antidepressant effect of moderate exercise (as part health-promoting lifestyle) may be triggered by regulating circulating level of interleukin-6 in adults with major depressive disorder, IL-6, as small proteins secreted from muscle tissue, increases with age in conjunction with the progression of sarcopenia; however, more evidences suggest that exercise training has positive effects on improving muscle mass and strength at any age and in addition reduces IL-6 in older adults with chronic diseases.<sup>43,44</sup> Chronic mild stress and high-fat Diet, associated with IL-6 in the hippocampus and prefrontal cortex of rats, are further associated with depression-like behaviors, Tang proposed that stress-inducible IL-6, generated in brown adipocytes via beta-3 adrenergic receptor (ADRB3) signaling, is necessary in stress hyperglycemia as a kind of metabolic adaptation enabling “fight or flight” response, stress management and social support to some extent relieve stress response and down regulate IL-6 level.<sup>45–48</sup> Nutritional-balanced diets are beneficial to health maintenance for human being, one previous study showed that the soybean and fish oil mixture, more than the fish oil alone, could be a complementary therapy to achieve a cytokine balance in ulcerative colitis. Another study conducted in children with cancer suggested that 56% of children were undernourished with higher tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and IL-6 levels, and the cytokine responses during chemotherapy were related to nutritional status for the greatly decreased IL-6 level in the well-nourished group.<sup>49,50</sup> These results strongly indicate that a nutritionally balanced diet with a health-promoting lifestyle may contribute to cytokine balance in older adults. Some other studies also find that horticultural therapy could reduce biomarkers of T-cell exhaustion which associated with IL-6 and social connectedness may serve as a modifiable factor for ameliorating increased IL-6 in older adults.<sup>51,52</sup> Based on the health-promoting lifestyle of aerobic exercise, stress management, nutritional-balanced diet, horticultural therapy, the LOD is improved ultimately accompanied by a decrease of IL-6. It is argued that the health-promoting lifestyle is a and being developed concept, this present study, employing a multidimensional scale for assessment for health-promoting lifestyle, is beneficial to understand the effects of health-promoting lifestyle comprehensively in health maintenance and prevention and treatment of disease and make up the deficiency of one-way assessment.

There may be some limitations in this study that need further consideration in future research, such as the inability to obtain a causal conclusion as a cross-sectional study, which can only be solved by rigorously designed prospective studies. Second, the analysis of the mediating effect of IL-6 between health-promoting lifestyles and LOD is not sufficiently profound due to insufficient exploration in this field; In particular, the mechanism about how SG induces LOD by regulating IL-6 is still unknown, based on previous research,<sup>53</sup> SG consists of self-identity, activation of psychodynamic system, behavioral approach, self-actualization, optimism, resilience, faith in life, etc., which may strengthen self-efficacy and ameliorate the stress response of the human body. Systematic verification is urgently needed in future research.

These limitations were offset by several strengths. This study sheds light on the pathological mechanisms of LOD from the perspectives of psychology and cytokines, which could provide a new framework for LOD prevention. The theoretical hypothesis proposed in this study may provide new directions for the prevention and treatment of LOD in older adults. Some researches reported that the disrupted intrinsic functional brain network may be the neural basis of late-life depression and lifestyle interventions benefits the brain function and neuron plasticity,<sup>54,55</sup> thus, future research could employ more specific methods, such as functional Magnetic Resonance Imaging (fMRI), to investigate the neural basis of the attenuating effect of health promoting lifestyles on LOD. The mediating effect of some other biomarkers,

such as cortisol, is also necessary to further elucidate the potential factors associated with the effect of health-promoting lifestyles on LOD.

## Conclusion

In summary, this study offers new insights into the pathology of LOD that health-promoting lifestyle, meaning in life, and IL-6 are predictors of LOD, and meaning in life and IL-6 are mediators between health-promoting lifestyle and LOD, that is, a health-promoting lifestyle may reduce LOD incidence by enhancing meaning in life and downregulating IL-6 level in older adults. This original study demonstrates that the cultivation of health promoting lifestyles may serve as an effective strategy to prevent LOD and presents a promising direction for further research in LOD care and rehabilitation.

## Abbreviations

IR, interpersonal relation; HR, health responsibility; SM, stress management; N, nutrition; PA, physical activity; SG, spiritual growth; PM, presence of meaning; SM, search for meaning; IL-6, interleukin-6; AS, anxiety/somatization; W, weight; CD, cognitive disorder; DV, diurnal variation; R, retardation; SD, sleep disturbance; H, hopelessness; HPLP-IIR, health-promoting lifestyle profile-II; revised, MLQ-C, meaning in life questionnaire-Chinese version; HAMD, Hamilton Depression Scale.

## Data Sharing Statement

The original contributions presented in this study are included in the article, and further inquiries can be directed to the corresponding author.

## Ethics Statement

Studies involving human participants were reviewed and approved by the Ethical Review Committee for Medical Research at No.904th Hospital, China. All participants provided written informed consent to participate in this study. This study was conducted in accordance with the principles of the Declaration of Helsinki.

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## Disclosure

The authors report no conflicts of interest in this work.

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